REMARKS

Claims 6-29 are pending in the present application. Applicants have amended claim 6, and added new claims 25-29. Support for these amendments can be found throughout the application as filed, e.g., at page 7, lines 5-20, and page 10, lines 8-17and 26-30. No new matter has been added.

Restriction Requirement

Applicants respectfully maintain their traversal of the restriction requirement. Applicants submit that the Examiner has not only failed to present reasons (as opposed to conclusions) as to why the inventions as claimed lack unity of invention, but also failed to present reasons for insisting upon restriction therebetween (e.g., no demonstration of undue burden). *See* M.P.E.P. § 808. Moreover, the restriction requirement fails to comply with the PCT rules and administrative instructions governing unity of invention.

As noted previously, the requirement of unity of invention referred to in PCT Rule 13.1 is satisfied when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features that define a contribution that the invention makes over the prior art. In the instant case, claims 6-20 by definition share the special technical features of claim 6, since all of claims 7-20 depend from claim 6. Thus, as all of these claims have the same objective (*i.e.*, identifying an agent having cellular anti-proliferative activity), all use the reagents defined in claim 6, and all include the steps of claim 6, the requirement for unity of invention is necessarily satisfied.

In support of her decision, the Examiner cites to PCT Article 17(3) as well as 37 C.F. R. §§ 1.475(b), 1.475 (d), and 1.476(a). However, none of these sections is applicable to and/or supports the **17-way** restriction alleged among claims 6-20 or the **15-way** restriction alleged among claims 21-24. Contrary to the Examiner's suggestion, claims 6-20 do not correspond to different "categories" of invention, nor do they constitute "multiple" processes or uses as defined in the cited sections. While dependent method claims 7-20 define further or alternate embodiments of the genus of independent method claim 6, claims 6-20 as a whole correspond to

a single invention, namely a single process for identifying an agent having cellular anti-proliferation activity using a fusion protein comprising Sp3 or a fragment thereof.

The PCT Administrative Instructions explicitly state in Annex B, Part 1(c)(i) that "[i]f the independent claims avoid the prior art and satisfy the unity of invention, **no problem of unity arises in respect to any claims that depend on the independent claims**. In particular, **it does not matter if a dependent claim itself contains a further invention**." (emphasis added) Accordingly, as the Examiner has failed to present evidence that claim 6 does not avoid the prior art, it is unclear how the Examiner can support restriction among independent claim 6 and dependent claims 7-20. In other words, the fact that the dependent claims set forth different combinations of reagents and/or further objectives is absolutely irrelevant to the issue of unity of invention.

With respect to the treatment of the alternatives set forth in claims 8-10 (such as a heterologous protein comprising "GAL4, LexA or tetracycline repressor" or a reporter gene comprising "luciferase, chloramphenicol acetyltransferase, beta-galactosidase, human growth hormone, or secreted alkaline phosphatase"), the Examiner's attention is respectfully directed to the PCT Administrative Instructions, Annex B, Part 1(f), which specifically state that "[w]herein a single claim defines alternatives, the requirement of a technical relationship and the same or corresponding special technical features shall be considered to be met when the alternatives are of a similar nature." In the instant case, no evidence has been presented that the claimed alternatives are sufficiently dissimilar as to warrant restriction. Furthermore, as the instantly claimed alternatives not only share a common property (*e.g.*, binding activity or reporter activity), but also would be expected by those in the art to behave in the same way in the context of the claimed invention (*i.e.*, could be substituted one for the other without affecting the intended result), they clearly are "of a similar nature." Thus, as the claimed alternatives have the requisite technical relationship, they necessarily meet the requirement for unity of invention and must be examined together.

Rejections under 35 U.S.C. § 112, First Paragraph -- Written Description

Claims 6-17, drawn to a heterologous protein GAL4 and a reporter gene encoding luciferase, were rejected at pages 3-8 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for allegedly containing subject matter not described in such a way as to reasonably convey possession of the claimed invention. In particular, the Examiner objected to the recitation of "an Sp3 fragment having transcriptional activity," and alleged that the instant specification describes only a limited class of fragments with the requisite activity and fails to describe the requisite structural/functional relationships of the other broadly claimed members of the genus or a representative number of such species.

The Applicants respectfully disagree. Nevertheless, to expedite prosecution, Applicants have amended claim 6 so that it is now directed to an Sp3 fragment "comprising at least one glutamine rich region of a TSA responsive domain of Sp3 and lacking at least part of the zinc finger region of Sp3." Applicants submit that the genus of fragments now recited in the claims is adequately described by the instant specification, as one of skill in the art could readily predict the sequences of the recited fragments.

Accordingly, the Applicants request reconsideration and withdrawal of the written description rejection in view of the amendments to the claims and the remarks herein.

Rejections under 35 U.S.C. § 112, First Paragraph -- Enablement

Claims 6-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to enable a method for identifying an agent having cellular anti-proliferation activity that utilizes any Sp3 from any species or any fragment of any Sp3 having transcriptional activation activity.

Applicants respectfully traverse. As noted above, to expedite prosecution Applicants have amended claim 6 to be directed to an Sp3 fragment "comprising at least one glutamine rich region of a TSA responsive domain of Sp3 and lacking at least part of the zinc finger region." With respect to the issue of "any" species of Sp3, a sequence comparison demonstrates that the two glutamine-rich domains of Sp3 are highly conserved across mammalian species; see Exhibit A attached hereto. In addition, a number of Sp3 sequences from other species were

known in the art at the time of filing, e.g., mammals such as mice and rats, and non-mammals such as drosophila and yeast. In support of this rejection, the Examiner cites Bowie et al. on page 13 for the proposition that altering a single amino acid in critical regions can abolish function. Applicants point out that presumably all Sp3 proteins of all species are functional in those species, so the teachings of Bowie et al. seem to be irrelevant to the present situation. Likewise, the citation of Scott et al. on page 14 does not support the rejection. The mere fact that one can't necessarily predict the function of a newly identified protein based solely on sequence comparisons does not meant that proteins that are known to function as Sp3 proteins in non human species can't be substituted for human Sp3 in the present methods. The reference to "Sp3" in the present claims denotes a protein that is indeed Sp3. If the Examiner is trying to make the point that one of ordinary skill in the art will not be able to ascertain whether any given protein is indeed an Sp3, Applicants note that such a position is contradicted by the Kollell et al. reference cited in the office action at page 13. Withdrawal of the rejection is therefore respectfully requested.

The Examiner further challenges the enablement of a method of identifying an agent having cellular anti-proliferation activity, noting that while the specification enables a method of identifying an agent that activates the Sp3 TSA response element, one cannot reasonably predict that the identified agents would have cellular anti-proliferation activity.

Applicants respectfully traverse. It is well established that histone deacetylase (HDAC) inhibitors such as TSA that induce transcription of the p21/WAF1/Cip1 gene have cellular anti-proliferation activity. A number of these HDAC inhibitors have been shown to have anticancer activity in clinical practice, see, e.g., Monneret, Eur. J. Med. Chem. 40:1-13 (2005), and Kim et al., J. Biochem. Mol. Biol. 36(1):110-119 (2003). Applicants have demonstrated that this TSA-activated transcription of the p21/WAF1/Cip1 gene is mediated by Sp3. Therefore, one of skill in the art would expect that an agent that activates the Sp3 TSA response element would also have cellular anti-proliferation activity. However, to advance prosecution, Applicants have amended claim 6 to recite "a method of "identifying an agent that activates an Sp3 TSA response element."

The Examiner stated at page 19 of the Office Action that

> ...no one skilled in the art would accept the assertion that a method of identifying an agent having cellular anti-proliferation activity based on the activation of Sp3 could be predictably used to identify an anti-cancer agent for cancer therapeutic strategies as inferred by the claim and as contemplated by the specification.

Applicants respectfully submit that this statement makes it clear that the Examiner is impermissibly reading limitations into the claims that are simply not there. The claim recites methods of "identifying an agent having cellular anti-proliferation activity." There is no requirement in the claim that the agent be useful in treating cancer in a human subject. Furthermore, as the specification points out at page 5, it is logical to believe that, since Sp3 activates p21/WAF1/Cip1 gene expression, and p21/WAF1/Cip1 expression leads to suppression of cell proliferation, then an agent that increases Sp3 activity would be expected to suppress cell proliferation. Applicants submit that the Examiner has not provided any scientific reasoning that controverts this logic, and therefore request that the Examiner reconsider and withdraw the enablement rejection.

Information Disclosure Statement

Upon reviewing the Form PTO-1449 attached to the Office Action, Applicants noticed that References AB and AF were not initialed by the Examiner. Applicants respectfully request that the Examiner consider said references and provide a new initialed Form PTO-1449.

Conclusion

For at least the reasons set forth herein, Applicants submit that the pending claims are patentable, and request immediate notification thereof.

Enclosed is a check for the Petition for Extension of Time fee, and a check for the additional claims fee. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket no. 14875-085001.

Respectfully submitted,

Date: July 24th, 2006

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